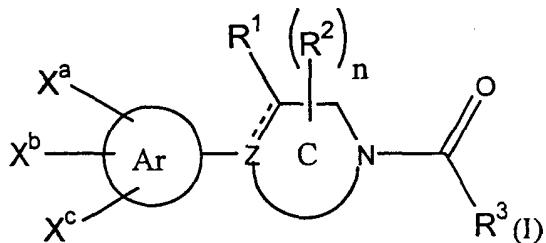


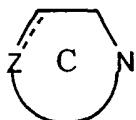
WHAT IS CLAIMED IS:

1. A compound of compound of formula I:



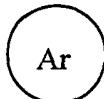
5 wherein:

Z is a carbon or nitrogen atom;

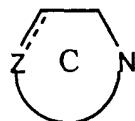


is a 4 to 7-membered azaheterocyclyl or a 4 to 7-membered azaheterocyclenyl group;

----- is a single or double bond, provided that when Z is a nitrogen atom, then ----- is a single bond;



10 is an aryl group, a monocyclic heteroaryl group, or a bicyclic azaheteroaryl group



which includes a first proximal ring that is attached to the moiety and a ring distal to said first ring, said distal ring including at least one nitrogen atom;

R¹ is hydrogen, -CH₂OR¹², -CH₂SR¹², -CO₂R¹³, -C(O)R¹³, or -CONR¹³R¹³;

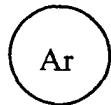
R² is hydrogen, alkyl, aralkyl, aralkenyl, aralkynyl, heteroaralkyl, heteroaralkenyl,

15 heteroaralkynyl, hydroxy, hydroxyalkyl, alkoxy, aryloxy, aralkoxy, acyl, aroyl, halo, nitro, cyano, carboxy, alkoxy carbonyl, aryloxy carbonyl, aralkoxy carbonyl, alkylsulfonyl, arylsulfonyl, heteroaryl sulfonyl, alkylsulfinyl, arylsulfinyl, heteroaryl sulfinyl, alkylthio, arylthio, heteroarylthio, aralkylthio, heteroaralkylthio, Y¹Y²N-, Y¹Y²N-alkyl-, Y¹Y²NCO- or Y¹Y²NSO₂-;

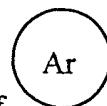
20 R³ is cycloalkyl, cycloalkenyl, heterocyclyl, heterocyclenyl, fused arylcycloalkyl, fused heteroaryl cycloalkyl, fused arylcycloalkenyl, fused heteroaryl cycloalkenyl, fused arylheterocyclyl, fused heteroaryl heterocyclyl, fused arylheterocyclenyl, fused

heteroarylheterocyclenyl, aryl, fused cycloalkenylaryl, fused cycloalkylaryl, fused heterocyclaryl, fused heterocyclenylaryl, heteroaryl, fused cycloalkylheteroaryl, fused cycloalkenylheteroaryl, fused heterocyclenylheteroaryl, fused heterocyclylheteroaryl; Xa, Xb, Xc are independently selected from hydrogen, R^4R^5N- , (hydroxy)HN-, (alkoxy)HN-,

5 R^6O- , R^4R^5NCO- , $R^4R^5NSO_2-$, R^6CO- , halo, cyano, nitro $R^7(O)C(CH_2)_q-$ and H_2N ;



and when is a bicyclic heteroaryl group, then Xc is a substituent that is at the alpha



position with respect to a nitrogen atom of said distal ring of and Xc is selected from the group consisting of H, hydroxy and H_2N- , (optionally substituted lower alkyl)HN (hydroxy)HN-, and (alkoxy)HN-;

10 R^4 and R^5 are independently H or optionally substituted lower alkyl, or one of R^4 and R^5 is H and the other of R^4 and R^5 is $R^7(O)CCH_2-$ or lower acyl;

R^6 is H, optionally substituted lower alkyl, lower acyl or $R^7(O)CCH_2-$;

R^7 is H, optionally substituted lower alkyl, alkoxy or hydroxy;

R^8 and R^9 taken together are $=NR^{10}$;

15 R^{10} is hydrogen, $R^{11}O_2C-$, $R^{11}O-$, HO-, cyano, $R^{11}CO-$, $HCO-$, lower alkyl, nitro, or Y^1aY^2aN- ;

R^{11} is alkyl, aralkyl, or heteroaralkyl;

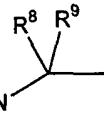
R^{12} is hydrogen, lower alkyl, aryl(lower alkyl), heteroaryl(lower alkyl), lower acyl, aroyl, or heteroaroyl;

20 R^{13} is hydrogen, lower alkyl;

Y^1 and Y^2 are independently hydrogen, alkyl, aryl, and aralkyl, or where the substituent is Y^1Y^2N- or Y^1Y^2N -alkyl- then one of Y^1 and Y^2 is acyl or aroyl and the other of Y^1 and Y^2 is hydrogen, alkyl, aryl, or aralkyl;

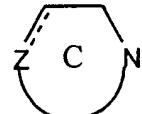
Y^1a and Y^2a are independently hydrogen or alkyl;

25 n is 1, 2, 3, or 4; or



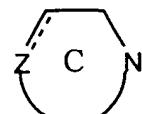
a pharmaceutically acceptable salt thereof, an N-oxide thereof, a hydrate thereof or a solvate thereof.

2. A compound according to claim 1 wherein Z is a carbon atom.

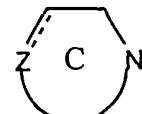


5 3. A compound according to claim 1 wherein Z is a carbon atom; is a 6-membered azaheterocyclyl or a 6-membered azaheterocyclenyl group; R¹ is selected from the group consisting of hydrogen -CH₂OR¹², -CH₂SR¹², -CO₂R¹³, -C(O)R¹³ and -CONR¹³R¹³; R¹² is hydrogen, lower alkyl, aryl(lower alkyl), or heteroaryl(lower alkyl); and R¹³ is hydrogen, or lower alkyl.

10



4. A compound according to claim 1 wherein Z is a carbon atom; is a 6-membered azaheterocyclenyl group; ----- is a double bond; and R¹ and R² are hydrogen.

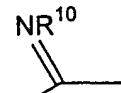


5. A compound according to claim 1 wherein Z is a carbon atom; is a 6-membered azaheterocyclyl group; and R¹ and R² are hydrogen.

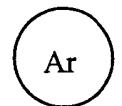
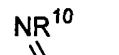
15 A compound according to claim 1 wherein R³ is optionally substituted (phenyl substituted phenyl), optionally substituted (heteroaryl substituted phenyl), optionally substituted (phenyl substituted heteroaryl) or optionally substituted (heteroaryl substituted heteroaryl).



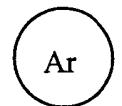
6. A compound according to claim 1 wherein is aryl or a monocyclic heteroaryl group; and X^C is selected from the group consisting of, R⁴R⁵N-, (hydroxy)HN-, (alkoxy)HN-,

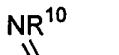


20 R⁶O-, R⁴R⁵NCO-, R⁴R⁵NSO₂-, R⁶CO-, halo, cyano, nitro R⁷(O)C(CH₂)_q-, and H₂N-



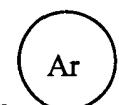
is an

7. A compound according to claim 1 wherein X^c is H_2N and  is an aryl group, a monocyclic heteroaryl group.

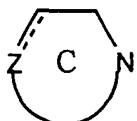


and is in the meta

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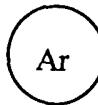


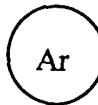
position with respect to the to the position of attachment of the

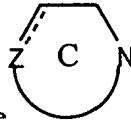


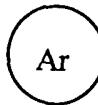
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moiety.



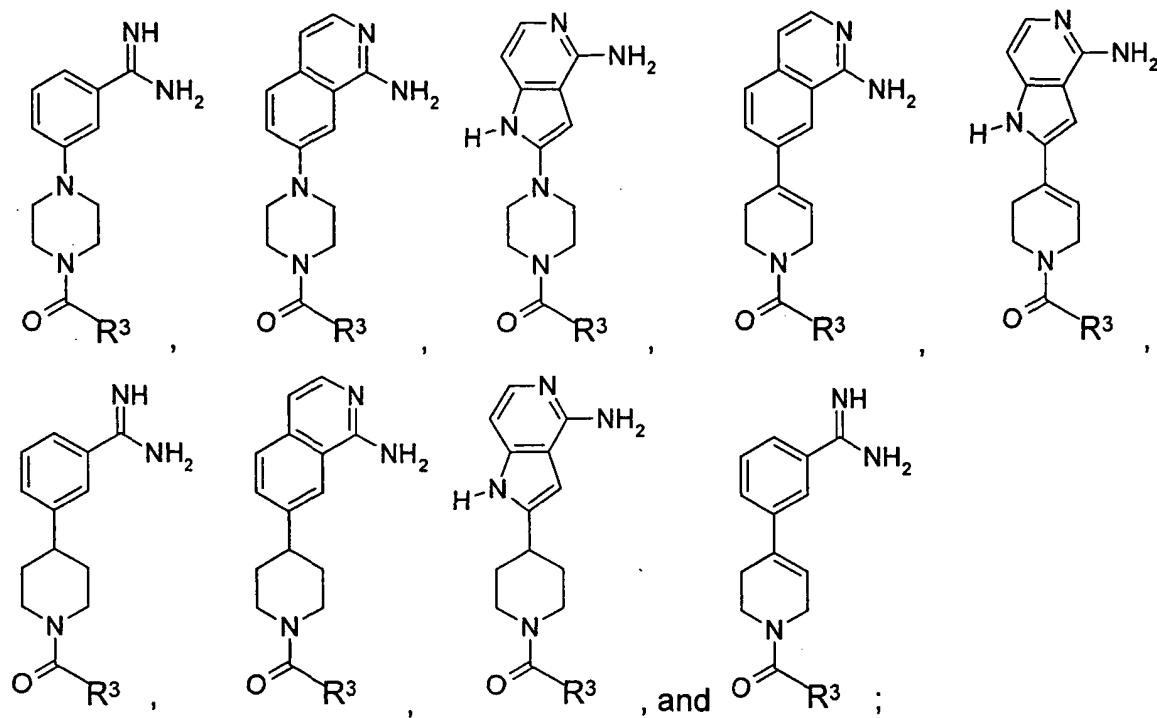
9. A compound according to claim 1 wherein  is a bicyclic azaheteroaryl group



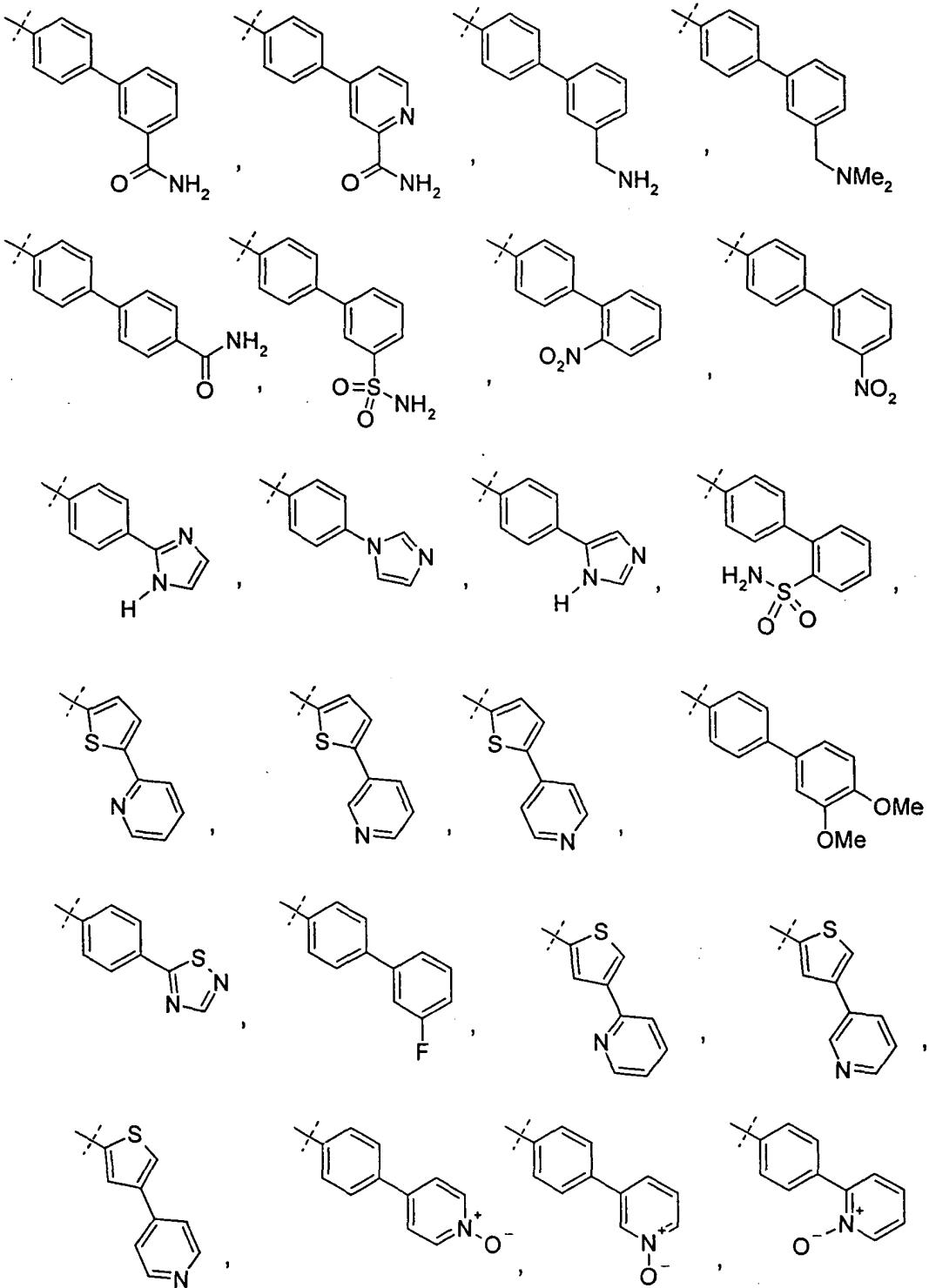
which includes a first proximal ring that is attached to the  moiety and a ring distal to said first ring; X^c is $\text{R}^4\text{R}^5\text{N}-$, $(\text{hydroxy})\text{HN}-$, or $(\text{alkoxy})\text{HN}-$, and X^c is in the alpha position with respect to a nitrogen atom in said distal ring.

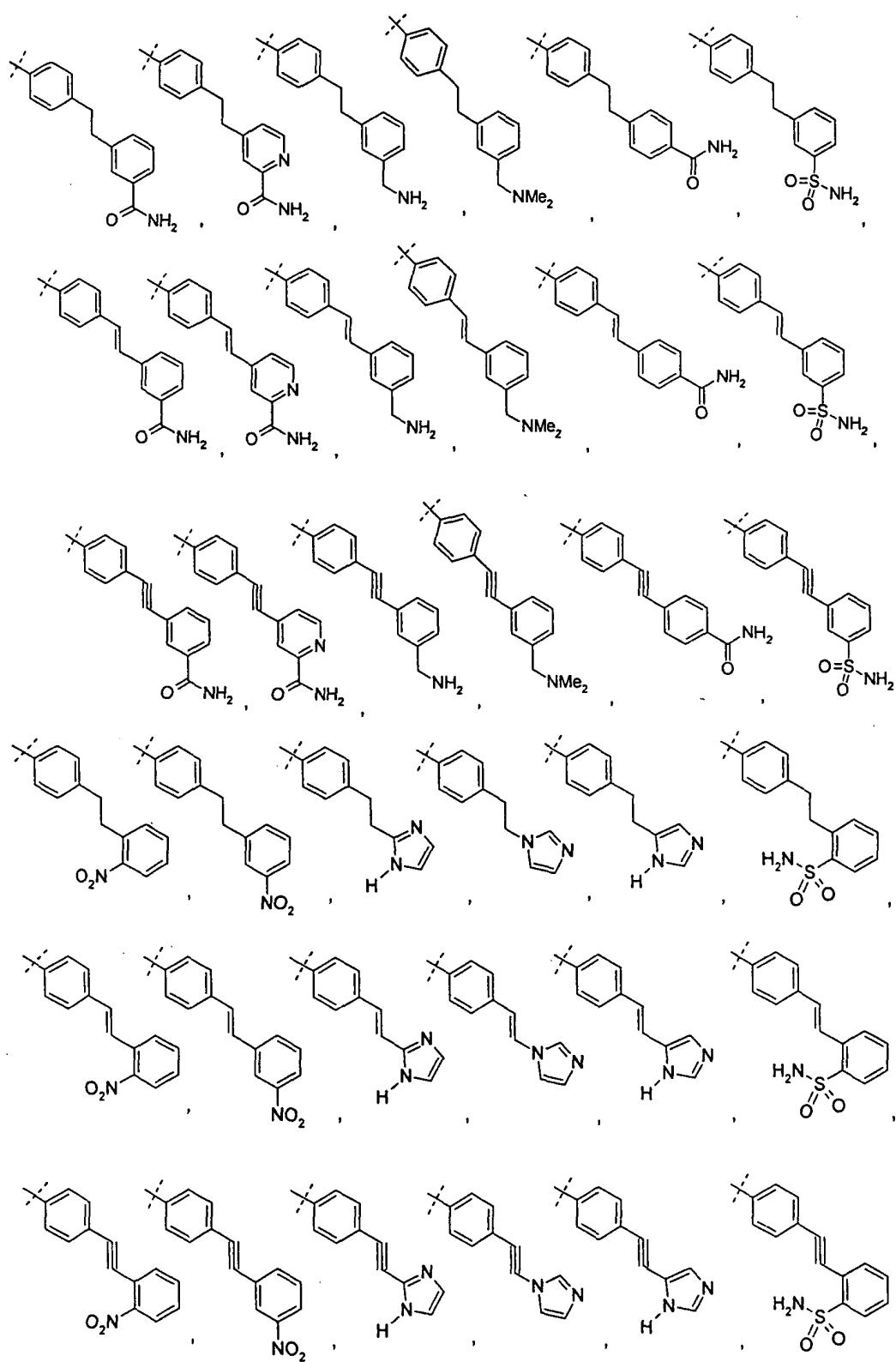
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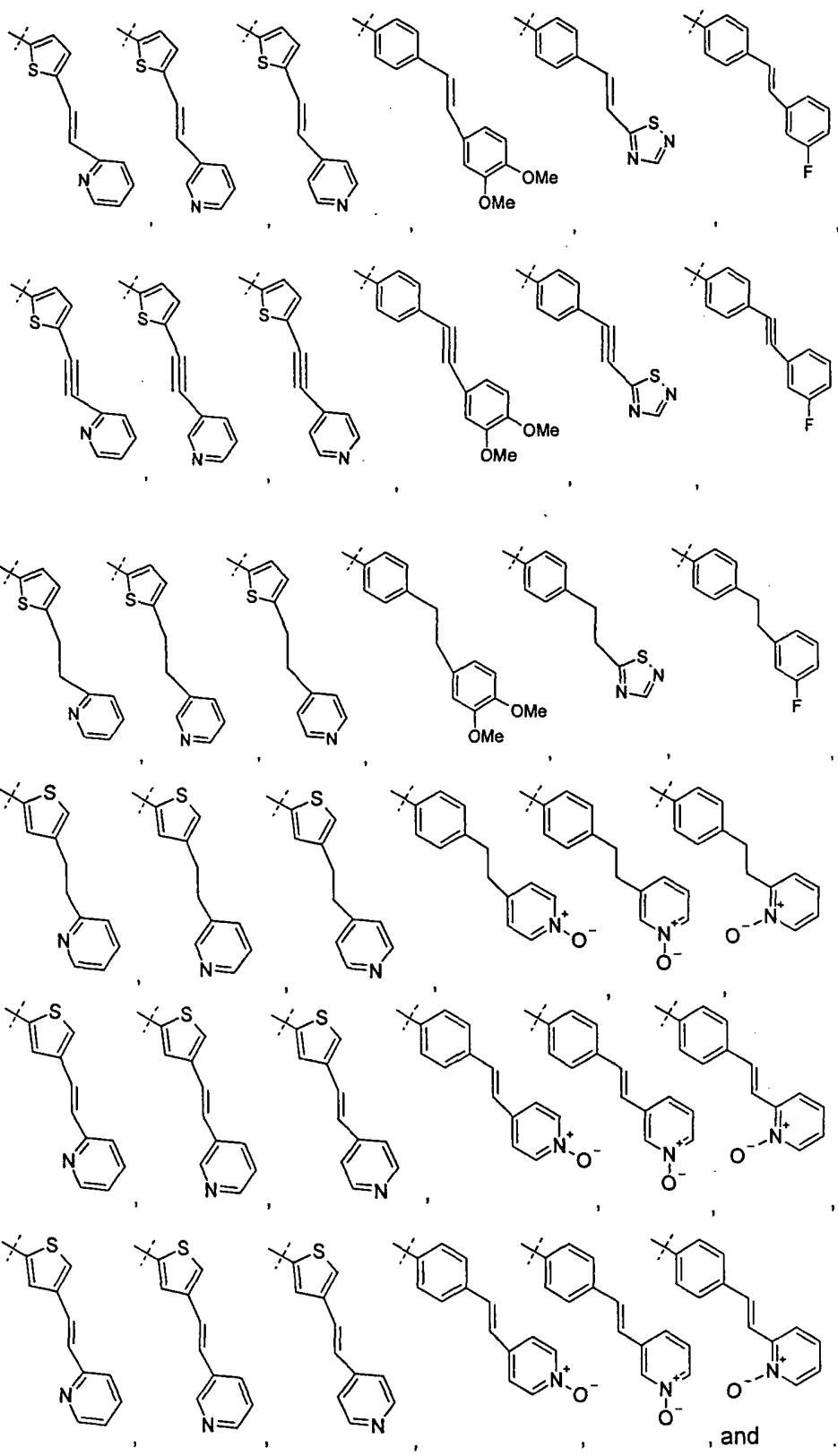
10. A compound according to claim 1, which is selected from the group consisting of



wherein R³ is selected from the group consisting of







11. A compound according to claim 1 selected from the group consisting of
3-[1-[4-(6-Oxo-1,6-dihydropyridine-3-yl)-benzoyl]-1,2,3,6-tetrahydropyridin-4-yl]benzamidine;
3-[1-[4-(1-Oxypyridin-2-yl)-benzoyl]-1,2,3,6-tetrahydropyridin-4-yl]benzamidine;
3-[1-[4-(1-Oxypyridin-4-yl)-benzoyl]-1,2,3,6-tetrahydropyridin-4-yl]benzamidine;
5 3-[1-[4-(6-Oxo-1,6-dihydropyridine-3-yl)-benzoyl]-piperidin-4-yl]benzamidine;
3-[1-[4-(1-Oxypyridin-4-yl)-benzoyl]-piperidin-4-yl]benzamidine;
3-[1-[4-(1-Oxypyridin-2-yl)-benzoyl]-piperidin-4-yl]benzamidine;
3-[1-(4-Pyridine-2-yl-benzoyl)-1,2,3,6-tetrahydropyridin-4-yl]benzamidine;
10 3-[1-(4-Pyridin-3-yl-benzoyl)-1,2,3,6-tetrahydropyridin-4-yl]benzamidine;
3-[1-(4-Pyridin-4-yl-benzoyl)-1,2,3,6-tetrahydropyridin-4-yl]benzamidine;
3-[1-[4-(5-Bromofuran-2-yl)-benzoyl]-1,2,3,6-tetrahydropyridin-4-yl]benzamidine;
3-[1-[4-(5-Chlorothiophen-2-yl)-benzoyl]-1,2,3,6-tetrahydropyridin-4-yl]benzamidine;
3-[1-(4-Thiophen-2-yl-benzoyl)-1,2,3,6-tetrahydropyridin-4-yl]benzamidine;
15 3-[1-[3-(5-Chlorothiophen-2-yl)-acryloyl]-1,2,3,6-tetrahydropyridin-4-yl]benzamidine;
3-[1-(4-[2-[2-Dimethylaminoethyl)methylamino]pyrimidin-4-yl]benzoyl)-1,2,3,6-
tetrahydropyridin-4-yl]benzamidine;
3-[1-[4-[2-(2-Dimethylaminoethyl)-6-oxo-1,6-dihydropyridin-3-yl]benzoyl]-1,2,3,6-
tetrahydropyridin-4-yl]benzamidine;
20 3-[1-(4-Pyrimidin-2-ylbenzoyl)-1,2,3,6-tetrahydropyridin-4-yl]benzamidine;
3-[1-(4-Pyrazin-2-ylbenzoyl)-1,2,3,6-tetrahydropyridin-4-yl]benzamidine;
3-[1-(4'-Sulfamoylbiphenyl-4-carbonyl)-1,2,3,6-tetrahydropyridin-4-yl]benzamidine;
3-[1-(3'-Sulfamoylbiphenyl-4-carbonyl)-1,2,3,6-tetrahydropyridin-4-yl]benzamidine;
3-[1-[4-(6-Methoxypyridazin-3-yl)benzoyl]-1,2,3,6-tetrahydropyridin-4-yl]benzamidine;
25 3-[1-[4-(6-Oxo-1,6-dihydropyridazin-3-yl)benzoyl]-1,2,3,6-tetrahydropyridin-4-yl]benzamidine;
3-[1-[4-(2-Aminopyrimidin-5-yl)benzoyl]-1,2,3,6-tetrahydropyridin-4-yl]benzamidine;
3-[1-[4-(6-Methoxypyridin-3-yl)benzoyl]-1,2,3,6-tetrahydropyridin-4-yl]benzamidine;
3-[1-(4-(Pyrimidin-5-ylbenzoyl)-1,2,3,6-tetrahydropyridin-4-yl]benzamidine;
30 3-[1-(4-Pyridin-2-ylbenzoyl)-piperidin-4-yl]benzamidine;
3-[1-(4-Pyridin-3-ylbenzoyl)-piperidin-4-yl]benzamidine;
3-[1-(4-Pyridin-4-ylbenzoyl)-piperidin-4-yl]benzamidine;
3-[1-[4-(6-Methoxypyridin-3-yl)benzoyl]-piperidin-4-yl]benzamidine;
3-[1-[4-(6-Methoxypyridazin-3-yl)benzoyl]-piperidin-4-yl]benzamidine;

3-[1-[4-(6-Oxo-1,6-dihydropyridazin-3-yl)benzoyl]-piperidin-4-yl]benzamidine;

5-[4-[4-(1-Aminoisoquinolin-7-yl)piperidine-1-carbonyl]phenyl]-1H-pyridin-2-one;

5-[4-(1-Aminoisoquinolin-7-yl)piperidine-1-carbonyl]-1'H-[2,3']bipyridinyl-6'-one;

[4-(1-Aminoisoquinolin-7-yl)piperidin-1-yl][2-fluoro-4-(6-methoxypyridin-3-yl)phenyl]methanone;

[4-(1-Aminoisoquinolin-7-yl)piperidin-1-yl](2-fluoro-4-pyridin-3-ylphenyl)methanone;

4'-[4-(1-Aminoisoquinolin-7-yl)piperidine-1-carbonyl]biphenyl-3-carboxylic acid amide;

[4-(1-Aminoisoquinolin-7-yl)piperidin-1-yl][5-(6-methoxypyridin-3-yl)thiophen-2-yl]]methanone;

10 5-[4-[4-(1-Aminoisoquinolin-7-yl)piperidine-1-carbonyl]-3-fluorophenyl]-1H-pyridin-2-one;

5-[5-[4-(1-Aminoisoquinolin-7-yl)piperidine-1-carbonyl]thiophen-2-yl]-1H-pyridin-2-one;

5-[4-[4-(1-Aminoisoquinolin-7-yl)-3,6-dihydro-2H-pyridine-1-carbonyl]phenyl]-1H-pyridin-2-one;

[4-(1-Aminoisoquinolin-7-yl)-3,6-dihydro-2H-pyridin-1-yl](4-pyridin-4-ylphenyl)methanone;

15 [4-(1-Aminoisoquinolin-7-yl)piperidin-1-yl][4-(6-methoxypyridin-3-yl)phenyl]methanone;

[4-(1-Aminoisoquinolin-7-yl)piperidin-1-yl](4-pyridin-3-ylphenyl)methanone;

[4-(1-Aminoisoquinolin-7-yl)piperidin-1-yl](6'-methoxy-[2,3']bipyridin-5-yl)methanone;

5-[4-[4-(4-Amino-1H-pyrrolo[3,2-c]pyridin-2-yl)piperidine-1-carbonyl]phenyl]-1H-pyridin-2-one;

20 5-[4-(4-Amino-1H-pyrrolo[3,2-c]pyridin-2-yl)piperidine-1-carbonyl]-1'H-[2,3']bipyridinyl-6'-one;

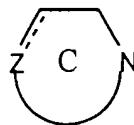
3-[1-(5-Phenylethyl-pyridine-3-carbonyl)-piperidin-4-yl]-benzamidine;

3-[1-(5-Phenylethynyl-pyridine-3-carbonyl)-1,2,3,6-tetrahydropyridin-4-yl]-benzamidine;

3-[1-(5-Phenylethynyl-pyridine-3-carbonyl)-piperidin-4-yl]-benzamidine; and

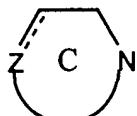
25 3-[4-(5-Phenylethyl-pyridine-3-carbonyl)-piperazin-1-yl]-benzamidine.

12. A compound according to claim 1 wherein



Z is a nitrogen atom; is a 6-membered azaheterocyclyl or a 6-membered azaheterocyclenyl group; is a single bond; and R¹ and R² are hydrogen.

13. A compound according to claim 1 wherein



Z is a nitrogen atom; is a 6-membered azaheterocyclyl or a 6-membered azaheterocyclenyl group; is a single bond; and R¹ is selected from the group consisting of hydrogen -CH₂OR¹², -CH₂SR¹², -CO₂R¹³, -C(O)R¹³ and -CONR¹³R¹³.

5

14. A compound according to claim 12 or 13 wherein

R³ is optionally substituted (phenyl substituted aralkyl), optionally substituted (heteroaryl substituted aralkyl), optionally substituted (phenyl substituted heteroaralkyl) or optionally substituted (heteroaryl substituted heteroaralkyl).

10

15. A compound according to claim 12 or 13 wherein

R³ is optionally substituted (phenyl substituted aralkenyl), optionally substituted (heteroaryl substituted aralkenyl), optionally substituted (phenyl substituted heteroaralkenyl) or optionally substituted (heteroaryl substituted heteroaralkenyl).

15

16. A compound according to claim 12 or 13 wherein

R³ is optionally substituted (phenyl substituted aralkynl), optionally substituted (heteroaryl substituted aralkynl), optionally substituted (phenyl substituted heteroaralkynl) or optionally substituted (heteroaryl substituted heteroaralkynl), (wherein the term "optionally substituted" before the term in the parenthesis, denote that the phenyl, heteroaryl, aralkynl, heteroaralkynl portions thereof could be further substituted as noted per their definitions).

17. A compound according to claim 1 selected from the group consisting of

3-[1-(5-Phenylethyl-pyridine-3-carbonyl)-piperidin-4-yl]-benzamidine;

25 3-[1-(5-Phenylethynyl-pyridine-3-carbonyl)-1,2,3,6-tetrahydropyridin-4-yl]-benzamidine;

3-[1-(5-Phenylethynyl-pyridine-3-carbonyl)-piperidin-4-yl]-benzamidine;

3-[1-[4-(6-Methoxypyridin-3-yl)benzoyl]-1,2,3,6-tetrahydropyridin-4-yl]-benzamidine;

3-[1-(4-(Pyrimidin-5-ylbenzoyl)-1,2,3,6-tetrahydropyridin-4-yl]-benzamidine;

3-[1-[4-(6-Methoxypyridazin-3-yl)benzoyl]-piperidin-4-yl]-benzamidine;

30 3-[1-[4-(1-Oxypyridin-2-yl)-benzoyl]-piperidin-4-yl]-benzamidine;

3-[1-(4-Pyridine-2-yl-benzoyl)-1,2,3,6-tetrahydropyridin-4-yl]benzamidine;
3-[1-(4-Pyridin-4-yl-benzoyl)-1,2,3,6-tetrahydropyridin-4-yl]benzamidine;
3-[1-(4-{2-[(2-Dimethylaminoethyl)methylamino]pyrimidin-4-yl}benzoyl)-1,2,3,6-tetrahydropyridin-4-yl]benzamidine; and
5 3-[4-(5-Phenylethyl-pyridine-3-carbonyl)-piperazin-1-yl]-benzamidine.

18. A compound according to claim 1 selected from the group consisting of
3-{1-[4-(1-Oxypyridin-4-yl)-benzoyl]-1,2,3,6-tetrahydropyridin-4-yl}benzamidine;
3-{1-[4-(6-Oxo-1,6-dihydropyridine-3-yl)-benzoyl]-piperidin-4-yl}benzamidine;
10 3-{1-[4-(1-Oxypyridin-4-yl)-benzoyl]-piperidin-4-yl}benzamidine;
3-{1-[4-(6-Oxo-1,6-dihydropyridine-3-yl)-benzoyl]-1,2,3,6-tetrahydropyridin-4-yl}benzamidine;
3-{1-[4-(6-Oxo-1,6 dihydropyridazin-3-yl)benzoyl]-1,2,3,6-tetrahydropyridin-4-yl}-benzamidine;
and
3-{1-[4-(6-Oxo-1,6-dihydropyridazin-3-yl)benzoyl]-piperidin-4-yl}benzamidine.

15 19. A method for treating a patient suffering from a disease state capable of being modulated by inhibiting tryptase activity comprising administering to said patient a pharmaceutically effective amount of a compound according to claim 1 or claim 17.

20 20. A method for preventing and treating an inflammatory diseases associated with tryptase activity comprising administering to said patient a pharmaceutically effective amount of a compound according to claim 1 or claim 17.

21. A method for preventing and treating late phase bronchoconstriction associated with 25 chronic asthma comprising administering to said patient a pharmaceutically effective amount of a compound according to claim 1 or claim 17.

22. A method according to claim 19 wherein said disease state is selected from the group 30 consisting of immunomediated inflammatory disorders associated with tryptase activity, such as rheumatoid arthritis, osteoarthritis, gouty arthritis, rheumatoid spondylitis, diseases of joint cartilage destruction, ocular conjunctivitis, vernal conjunctivitis, inflammatory bowel disease, asthma, allergic rhinitis, and interstitial lung diseases.

23. A method according to claim 19 wherein said disease state is selected from the group consisting of fibrosis, scleroderma, pulmonary fibrosis, liver cirrhosis, myocardial fibrosis, neurofibromas, hypertrophic scars, and various dermatological conditions, for example, atopic 5 dermatitis and psoriasis.

24. A method according to claim 19 wherein said disease state is selected from the group consisting of myocardial infarction, stroke, angina and other consequences of atherosclerotic plaque rupture; as well as periodontal disease, diabetic retinopathy, tumor growth, anaphylaxis, 10 multiple sclerosis, peptic ulcers, and syncytial viral infections.

25. A method of inhibiting tryptase activity comprising contacting a tryptase inhibitory amount of a compound of according to claim 1 or claim 17 with a composition containing tryptase. 15

26. A method of treating a patient suffering from a disease state capable of being modulated by inhibiting tryptase activity comprising administering to a patient, in need thereof, a compound according to claim 1 or claim 17 or a pharmaceutically acceptable salt thereof, and optionally at least one compound selected from the group consisting of a β -adrenergic agonist compound, an 20 anti-inflammatory corticosteroid compound, an anticholinergics compound, and an anti-inflammatory compound, or a pharmaceutically acceptable salt thereof, wherein said β -adrenergic agonist compound is selected from the group consisting of albuterol, terbutaline, formoterol, fenoterol, and prenalone; said anti-inflammatory corticosteroid compound is selected 25 from the group consisting of beclomethasone, triamcinolone, flurisolide, and dexamethasone; said anticholinergics compound is ipratropium bromide; and said anti-inflammatory compound is selected from the group consisting of sodium cromoglycate and nedocromil sodium.

27. A pharmaceutical composition comprising a pharmaceutically acceptable amount of the compound according to claim 1 and a pharmaceutically acceptable carrier. 30

28. A method for treating a patient suffering from a physiological condition capable of being modulated by inhibiting activity of Factor Xa comprising administering to said patient a pharmaceutically effective amount of the compound according to claim 2 or 18.

5 29. The method according to claim 28 wherein the physiological condition is venous vasculature, arterial vasculature, abnormal thrombus formation, acute myocardial infarction, unstable angina, thromboembolism, acute vessel closure associated with thrombolytic therapy, percutaneous transluminal coronary angioplasty, transient ischemic attacks, stroke, intermittent claudication or bypass grafting of the coronary or peripheral arteries, vessel luminal narrowing, 10 restenosis post coronary or venous angioplasty, maintenance of vascular access patency in long-term hemodialysis patients, pathologic thrombus formation occurring in the veins of the lower extremities following abdominal, knee and hip surgery, a risk of pulmonary thromboembolism, or disseminated systemic intravascular coagulopathy occurring in vascular systems during septic shock, certain viral infections or cancer.

15 30. The method according to claim 28 wherein the physiological condition is abnormal thrombus formation, acute myocardial infarction, unstable angina, thromboembolism, acute vessel closure associated with thrombolytic therapy, transient ischemic attacks, intermittent claudication or bypass grafting of the coronary or peripheral arteries, restenosis post coronary or 20 venous angioplasty, pathologic thrombus formation occurring in the veins of the lower extremities following abdominal, knee and hip surgery or a risk of pulmonary thromboembolism.

25 31. The method according to claim 28 wherein the physiological condition is stroke, vessel luminal narrowing, maintenance of vascular access patency in long-term hemodialysis patients, or disseminated systemic intravascular coagulopathy occurring in vascular systems during septic shock, certain viral infections or cancer.

32. A method of inhibiting Factor Xa comprising contacting a Factor Xa inhibitory amount of a compound according to claim 2 or claim 18 with a composition containing Factor Xa.

33. A method of inhibiting the formation of thrombin comprising contacting Factor Xa inhibitory amount of a compound according to claim 2 or claim 18 with a composition containing Factor Xa.

5 34. A method for treating a patient suffering from a physiological condition capable of being modulated by directly inhibiting activity of both Factor Xa and Factor IIa (thrombin) comprising administering to said patient a pharmaceutically effective amount of the compound according to claim 2 or claim 18.

10 35. A method of treating a patient suffering from a disease state capable of being modulated by inhibiting Factor Xa activity comprising administering to a patient, in need thereof, a compound according to claim 2 or claim 18 or a pharmaceutically acceptable salt thereof, and optionally at least one compound selected from the group consisting of a cardioprotective agent, a direct thrombin inhibitor, an anticoagulant, an antiplatelet agent or fibrinolytic agent.